



**EXPEDITED PROCEDURE - EXAMINING GROUP 1614**

**S/N 09/589,476**

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant:	Dennis A. Carson et al.	Examiner:	Jerome D. Goldberg
Serial No.:	09/589,476	Group Art Unit:	1614
Filed:	June 7, 2000	Docket:	103.021US1
Title:	<u>USE OF ETODOLAC IN THE TREATMENT OF CANCER</u>		

**DECLARATION UNDER 37 C.F.R. § 1.132**

Box AF  
Commissioner for Patents  
Washington, D.C. 20231

Sir:

I, Carlos J. Carrera, declare and say:

1. I am presently an Associate Clinical Professor in the Department of Medicine at the University of California San Diego. I am also a Staff Physician at the Veterans Affairs San Diego Medical Center (VASDMC). I am the author of more than 50 research papers in peer-reviewed journals and books in the subjects of purine metabolism and antimetabolite chemotherapy of lymphoid malignancies (leukemias and lymphomas). I am a named inventor on 5 issued U.S. patents. I have practiced and/or performed research in the area of cancer treatment for 22 years. In my practice I have extensive experience with treatment of cancers such as chronic leukemias and other cancers of the blood and lymphatic system.
2. I have no direct financial interest or any other beneficial interest in the issuance of U.S. Patent Application Serial No. 09/589,476. I am a consultant for Salmedix, Inc., a licensee of U.S. Patent Application Serial No. 09/589,476.
3. I graduated from the University Of Cincinnati College Of Medicine, received specialty training in Internal Medicine at Mt. Zion Hospital (San Francisco), and received subspecialty training in Hematology/Oncology at the University of California San Francisco. I am certified by the American Board of Internal Medicine in both Hematology and Oncology. I am licensed to practice medicine in the State of California.

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4. I have reviewed U.S. Patent Application Serial No. 09/589,476, the Office Action mailed July 25, 2002, and the response filed herewith, and make this declaration in support of the patentability of the pending claims.

5. In the Office Action mailed July 25, 2002, the Examiner has provisionally rejected claims 1, 3, 4, 11, 13, 14, 26-29, 34, and 35 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over the claims of U.S. Application Serial No. 09/360 020. The Examiner asserts that although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are directed to treating multiple myeloma (MM) and the claims of Application Serial No. 09/360 020 are directed to treating leukemia. The Examiner's rejection is based on the Applicants' remark in Paper No. 10, page 4, lines 4 and 5 that "both chronic lymphocytic leukemia and multiple myeloma can be considered leukemias". Thus, the Examiner concluded that "claims to treating leukemia are not patentably distinct from claims to treating a form of leukemia, i.e. multiple myeloma." (See Office Action mailed July 25, 2002, page 2, last paragraph.)

6. Although in some contexts Applicants' statement may be considered correct, as a practitioner in the specialty of Hematology and Oncology, I contend that Applicants' statement, "both chronic lymphocytic leukemia (CLL) and multiple myeloma (MM) can be considered leukemias" is incorrect. MM is a neoplastic disease of malignant plasma cells which, despite the name, are rarely seen in the circulating blood. Rather, the growth of MM cells produces tumors, marrow infiltration, excess monoclonal immunoglobulin production, lytic bone lesions and osteoporosis, hypercalcemia, and kidney disease. In contrast, the clinically defining hallmark of lymphoid leukemias, including CLL, is the accumulation of neoplastic leukocytes in the circulating blood, as well as in lymph glands and marrow. The Examiner's conclusion that MM is a leukemia is in error. Thus, one skilled in the art would not consider MM to be a leukemia in the context of how the disease is treated.

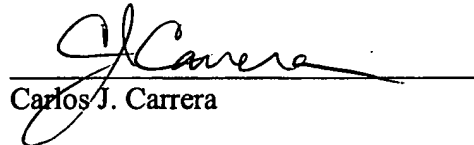
7. My conclusions are based on the fact that none of the conventional classification systems for lymphoid neoplasms describe MM as a leukemia (World Health Organization, Revised European-American Lymphoma Classification, International Working Formulation). In addition to obvious clinical and taxonomic differences, there is ample epidemiological, genetic

and pharmacodynamic evidence that CLL and MM are distinct cancers (Williams Hematology, 6th edition; Beutler, E, Coller, BS, Lichtman, MA, Kipps, TJ, and Seligsohn, U editors; McGraw-Hill 2001 New York, pp.1163-1164, 1279-1281). Environmental factors do not appear to play a role in the pathogenesis of CLL, whereas radiation and chemical exposure are known to be associated with the development of MM. Chromosome abnormalities that are frequent (>50%) in CLL (13q14-23.1, trisomy 12, del 11q22.3-q23.1, del 6q21-q23, abnormalities of 14q) are not reported as recurring karyotype changes in MM. The tumor suppressor gene p53 is rarely mutated in CLL except at end-stage, whereas p53 mutation or deletion occurs in over 50% of MM. Thus, it is erroneous to assert that MM can be considered a leukemia, as is CLL, as this obscures the many genetic, biologic, and drug response differences between these cancers.

8. It is my opinion, based on the different etiologies of leukemias and MM and past experience treating those diseases, that a person skilled in the art would not be inclined to infer or expect that multiple myeloma could be successfully treated with etodolac or novel drugs, such as etodolac analogues just because they were shown to be active in leukemia, especially chronic lymphatic leukemias (e.g., CLL, hairy cell leukemia).

9. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statement may jeopardize the validity of the application or any patent issuing thereon.

March 11, 2003  
Date

  
Carlos J. Carrera